ACTİVE MEMBRANE CONDUCTİVİTY
&
ACTİON POTENTİAL

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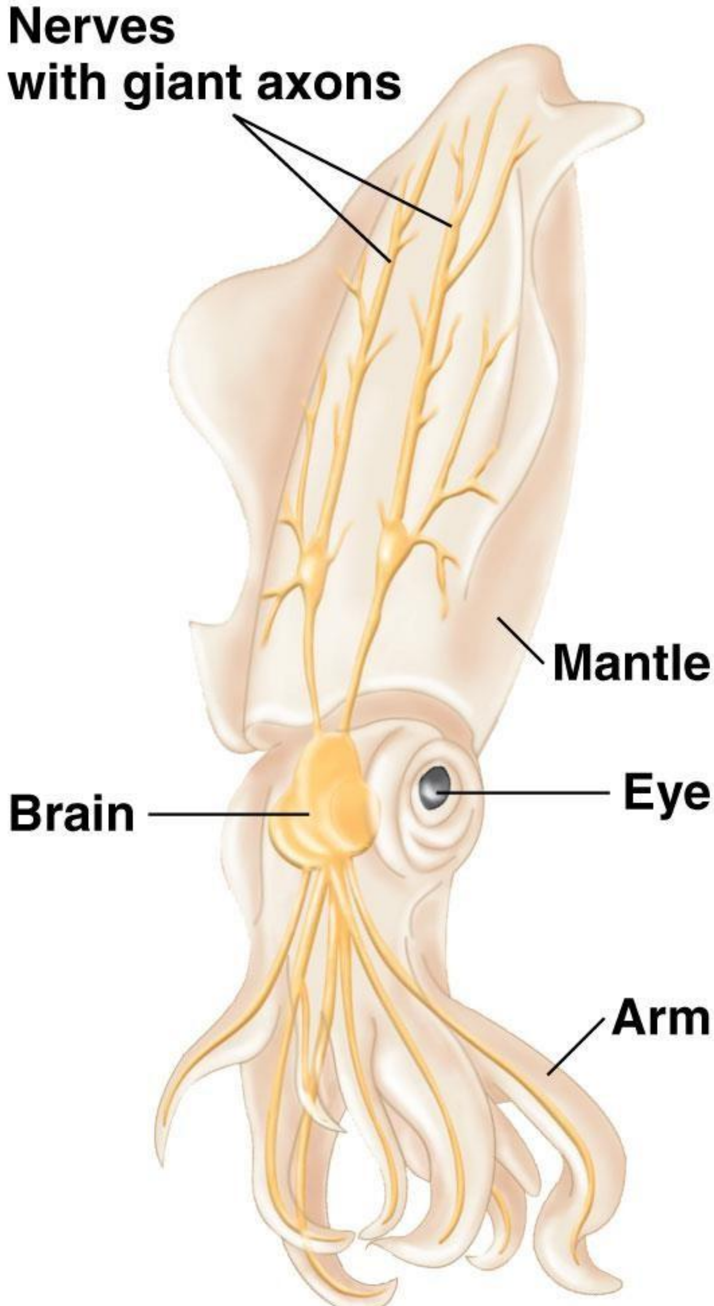
The Nobel Prize in Physiology or Medicine 1963 was awarded jointly to Sir John Carew Eccles, Alan Lloyd Hodgkin and Andrew Fielding Huxley "for their discoveries concerning the ionic mechanisms involved in excitation and inhibition in the peripheral and central portions of the nerve cell membrane".


Erwin Neher

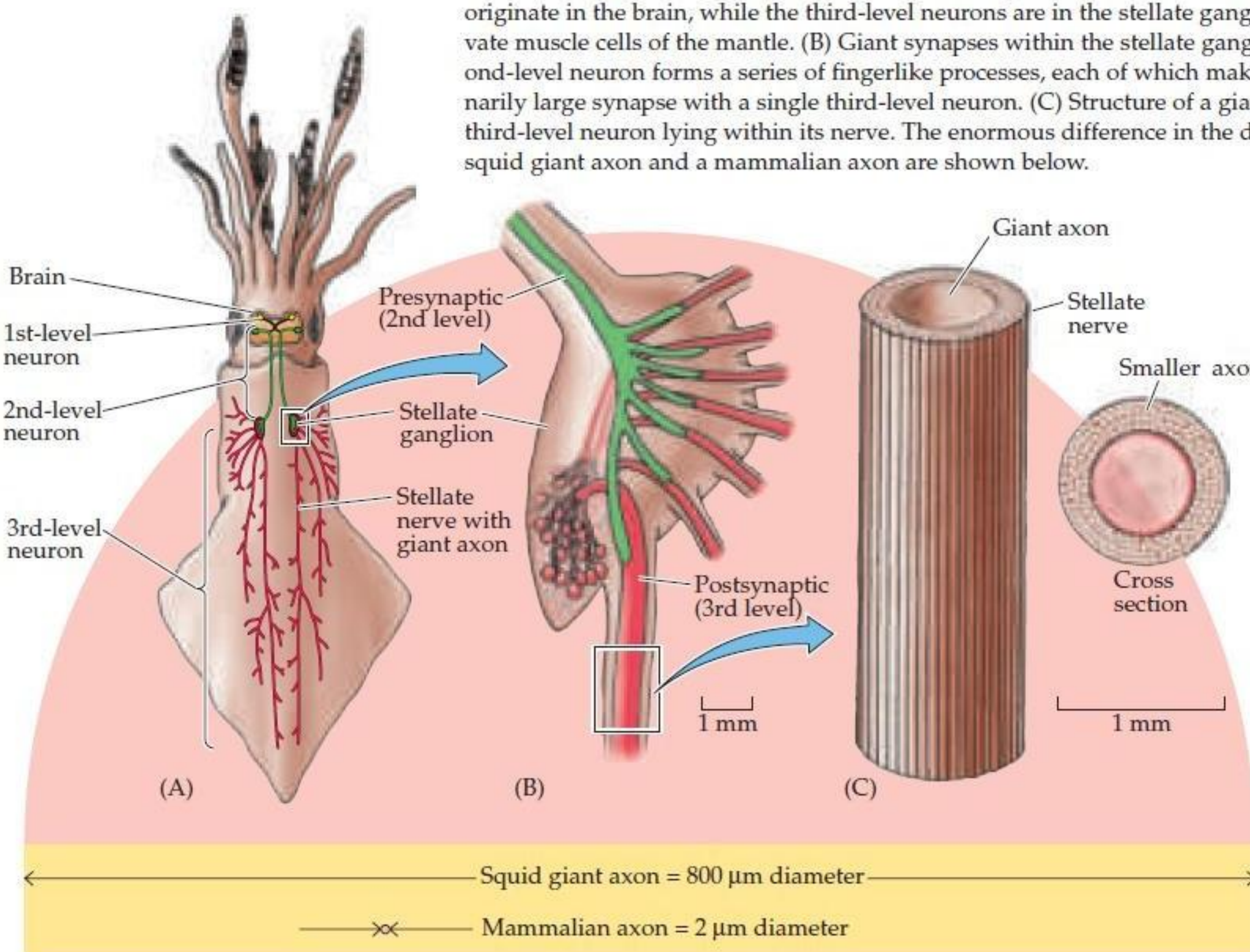

Bert Sakmann

The Nobel Prize in Physiology or Medicine 1991 was awarded jointly to Erwin Neher and Bert Sakmann *"for their discoveries concerning the function of single ion channels in cells"*

Squid


Nerves
with giant axons
Mantle
Eye
Brain
Arm

(A) Diagram of a squid, showing the location of its giant nerve cells. Different colors indicate the neuronal components of the escape circuitry. The first- and second-level neurons originate in the brain, while the third-level neurons are in the stellate ganglion and innervate muscle cells of the mantle. (B) Giant synapses within the stellate ganglion. The second-level neuron forms a series of fingerlike processes, each of which makes an extraordinarily large synapse with a single third-level neuron. (C) Structure of a giant axon of a third-level neuron lying within its nerve. The enormous difference in the diameters of a squid giant axon and a mammalian axon are shown below.



Extracellular and Intracellular Ion Concentrations

	CONCENTRATION (M*M*)	
ION	INTRACELLULAR	EXTRACELLULAR
Squid neuron		
Potassium (K^+)	400	20
Sodium (Na^+)	50	440
Chloride (Cl^-)	40–150	560
Calcium (Ca^{2+})	0.0001	10
Mammalian neuron		
Potassium (K^+)	140	5
Sodium (Na^+)	5–15	145
Chloride (Cl^-)	4–30	110
Calcium (Ca^{2+})	0.0001	1–2

NEUROSCIENCE 5e, **Table 2.1**

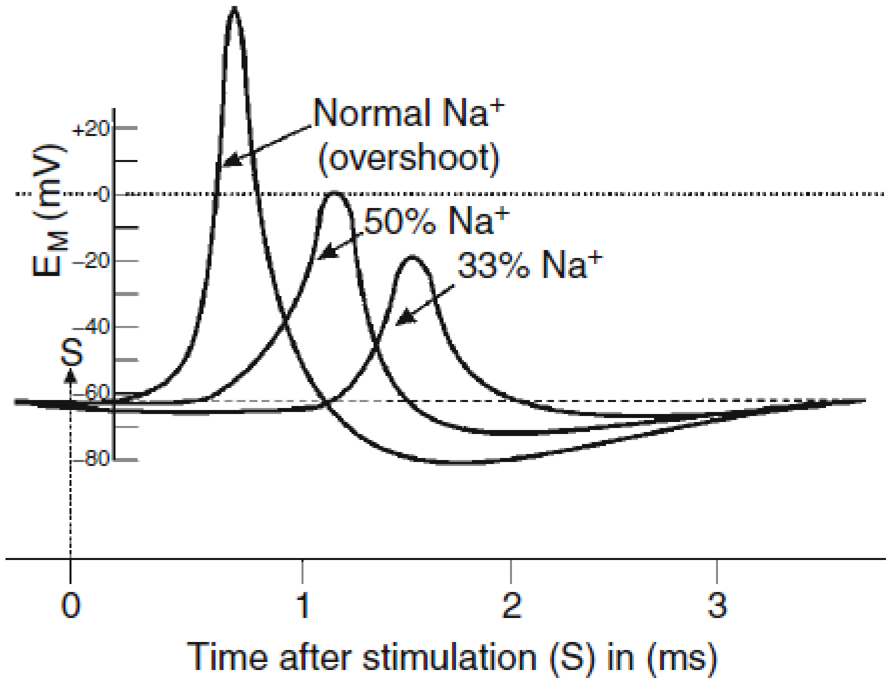
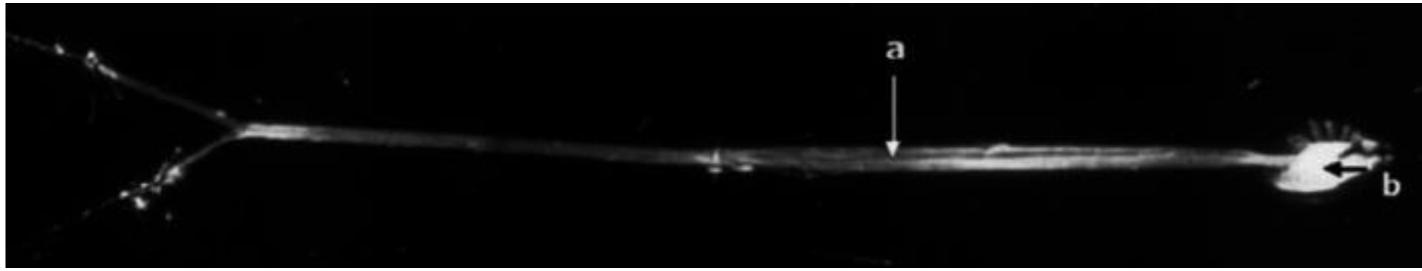
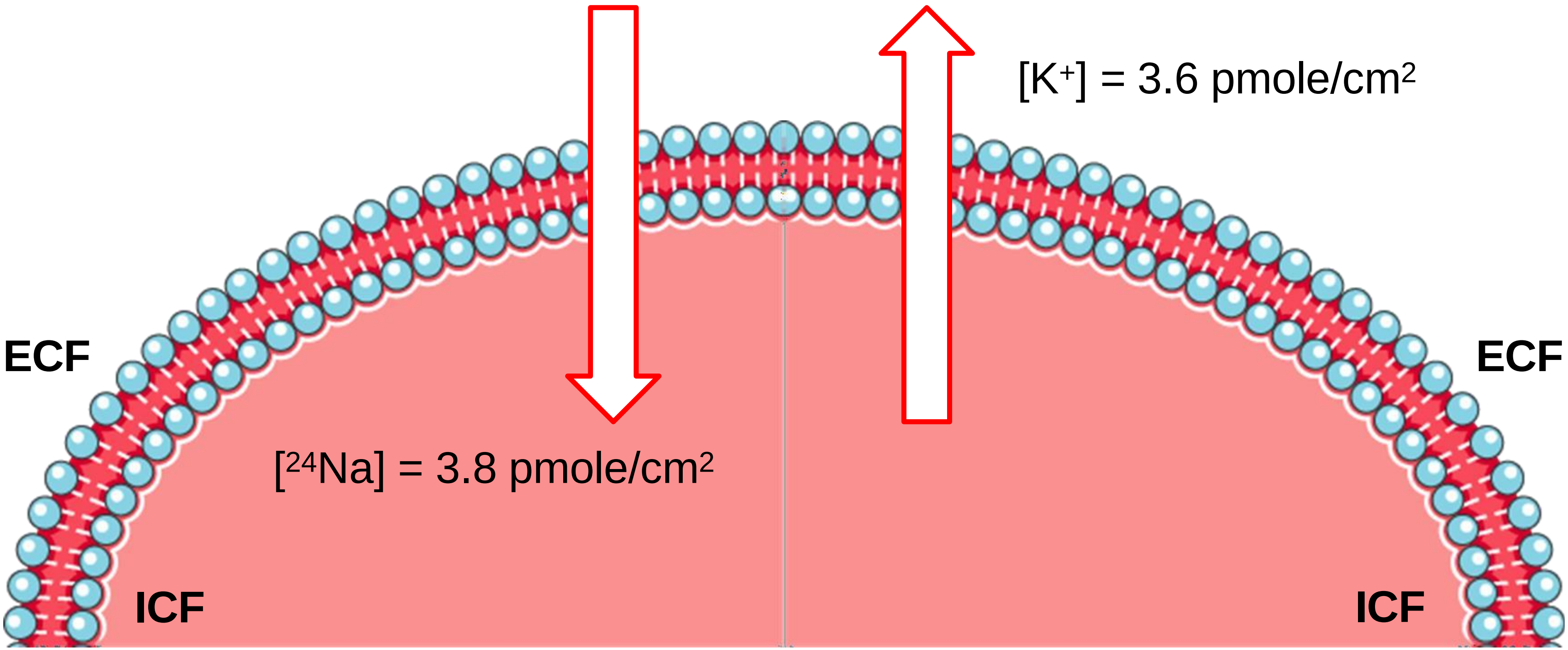
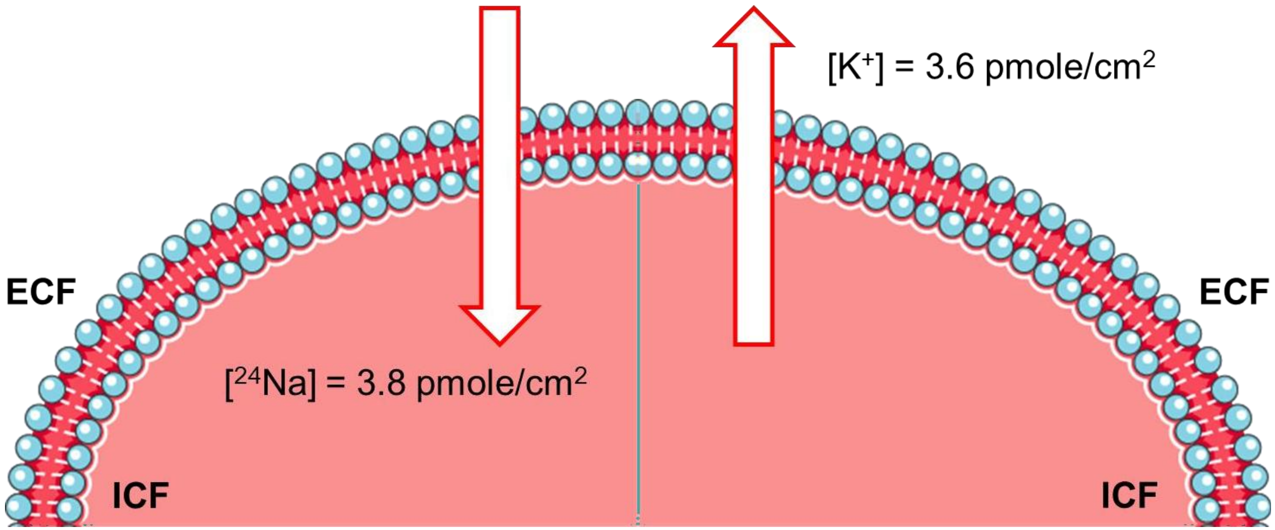


Illustration of the squid giant axon action potential and its dependence on external Na^+. The resting membrane potential (E_M) is about –60 mV. Following stimulation (S), the initial Na^+-dependent depolarization phase of the action potential that rises above 0 mV (overshoot) is gradually reduced in amplitude and delayed in time with reduction in extracellular Na^+. Similar experiments were originally conducted by Hodgkin, Huxley, and Katz in the 1930s/1950s using the voltage clamp technique (Section 16.5.1.1).


a
b


[K+] = 3.6 pmole/cm2
ECF
ECF
[24Na] = 3.8 pmole/cm2
ICF
ICF



$$C_m = 1\ \mu\text{F/cm}^2$$

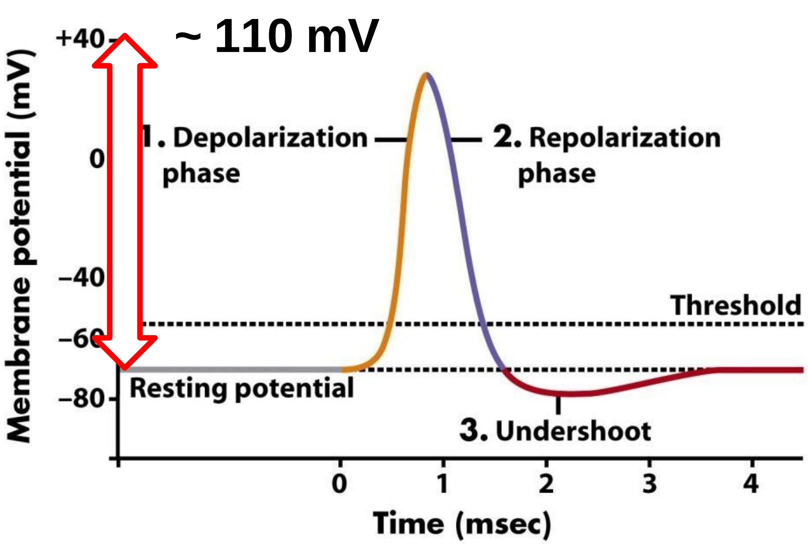
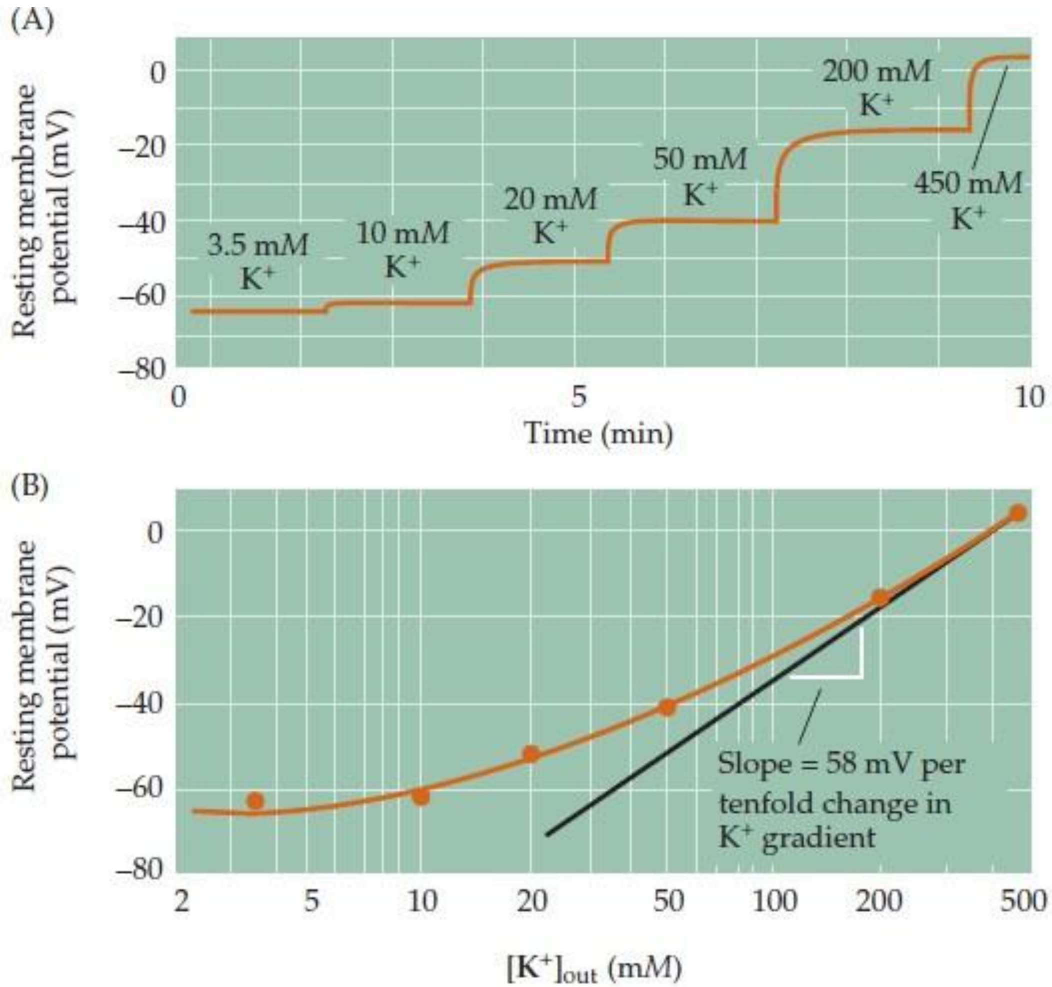


Figure 45-5 Biological Science, 2/e

$$\Delta q = C_m \cdot \Delta V = \left(10^{-6}\ \mu\text{F/cm}^2\right) \cdot 0.11\ V$$

$$\Delta q = 1.1 \times 10^{-7}\ \text{C/cm}^2$$

$$\boxed{\Delta q_{Na} = \frac{1.1 \times 10^{-7}\ \text{C/cm}^2}{96500\ \text{C/mole}} = 1.14\,\frac{pmole}{cm^2}}$$



Experimental evidence that the resting membrane potential of a squid giant axon is determined by the K^+ concentration gradient across the membrane. (A) Increasing the external K^+ concentration makes the resting membrane potential more positive. (B) Relationship between resting membrane potential and external K^+ concentration, plotted on a semi-logarithmic scale. The straight line represents a slope of 58 mV per tenfold change in concentration, as given by the Nernst equation. (After Hodgkin and Katz, 1949.)

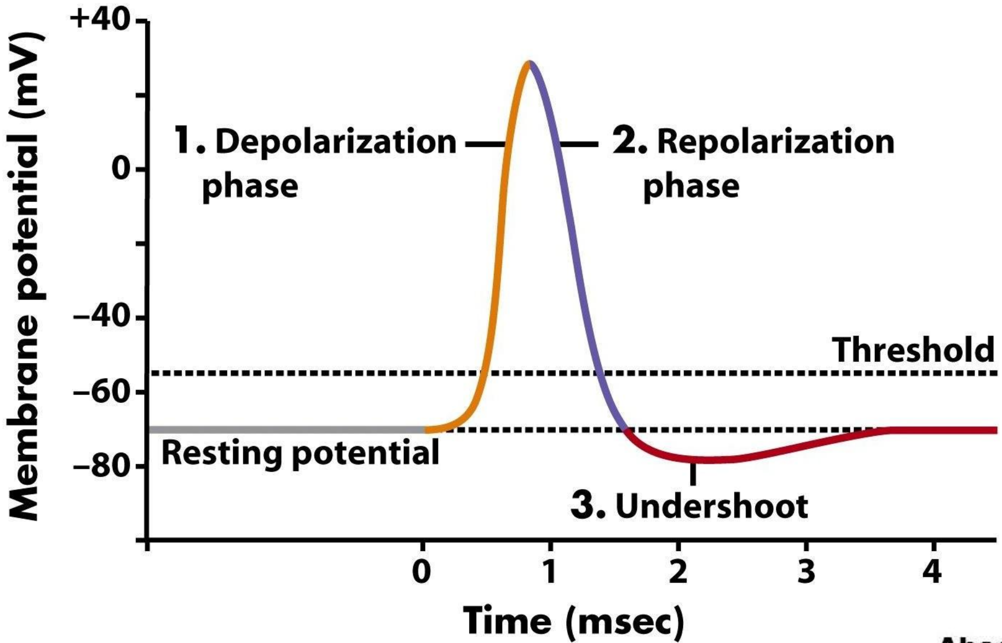
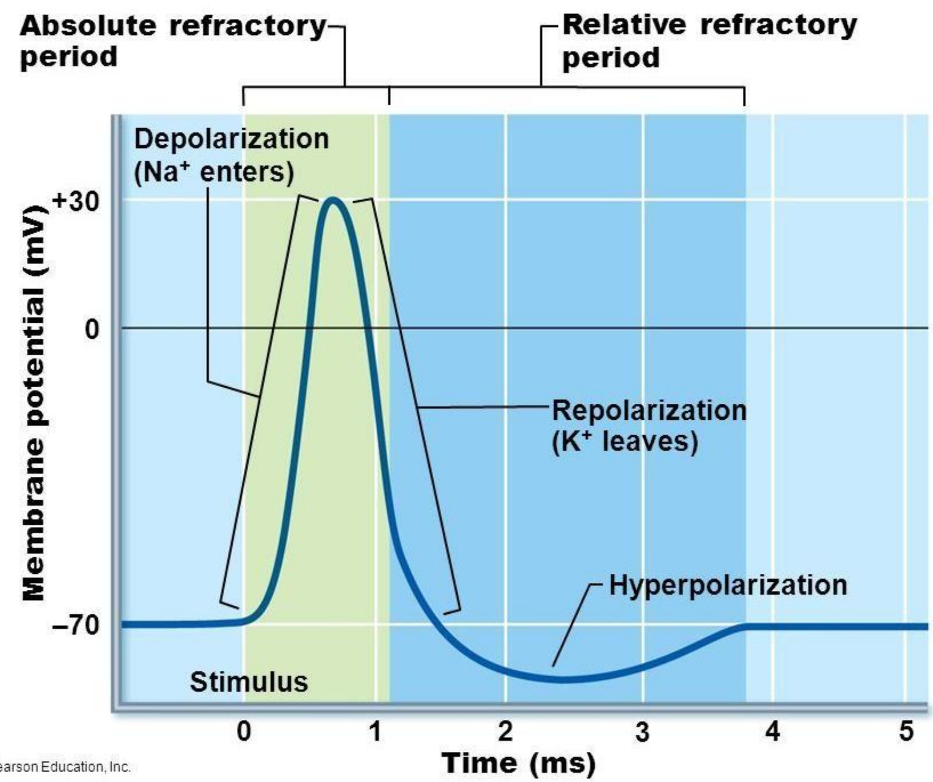
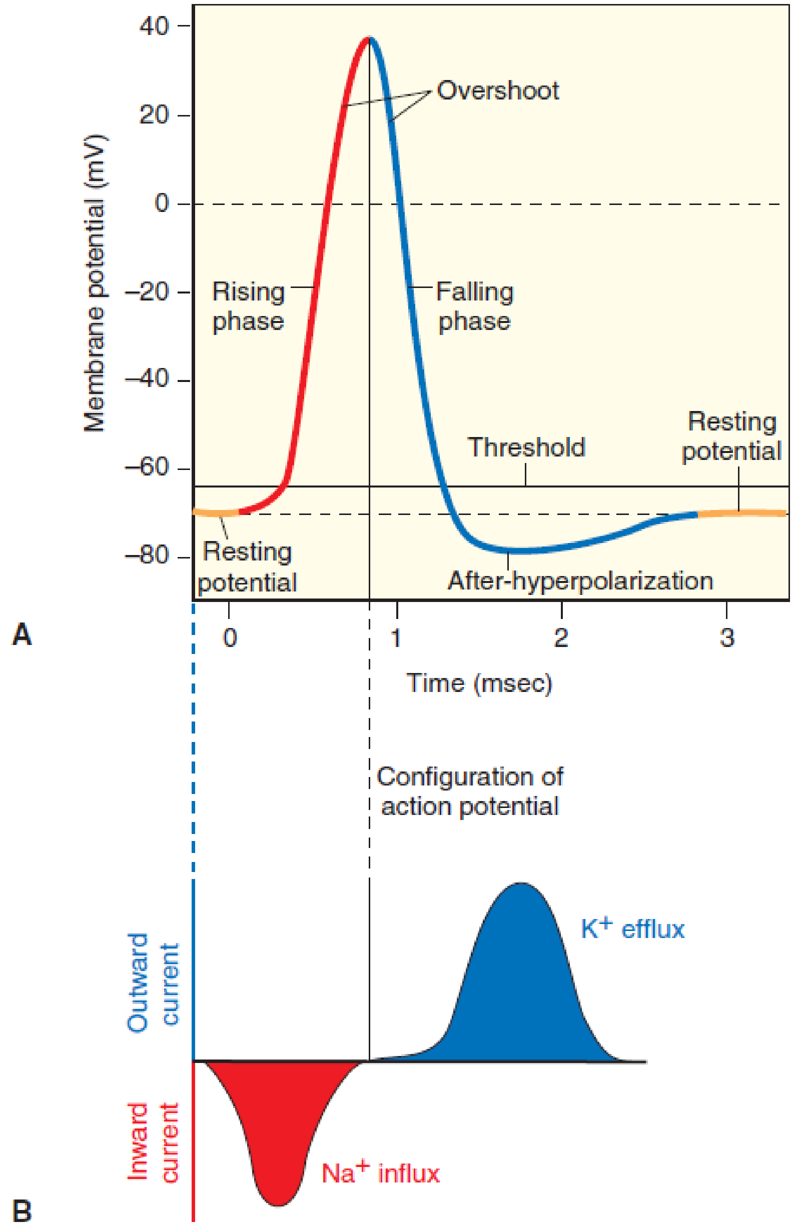


Figure 45-5 Biological Science, 2/e

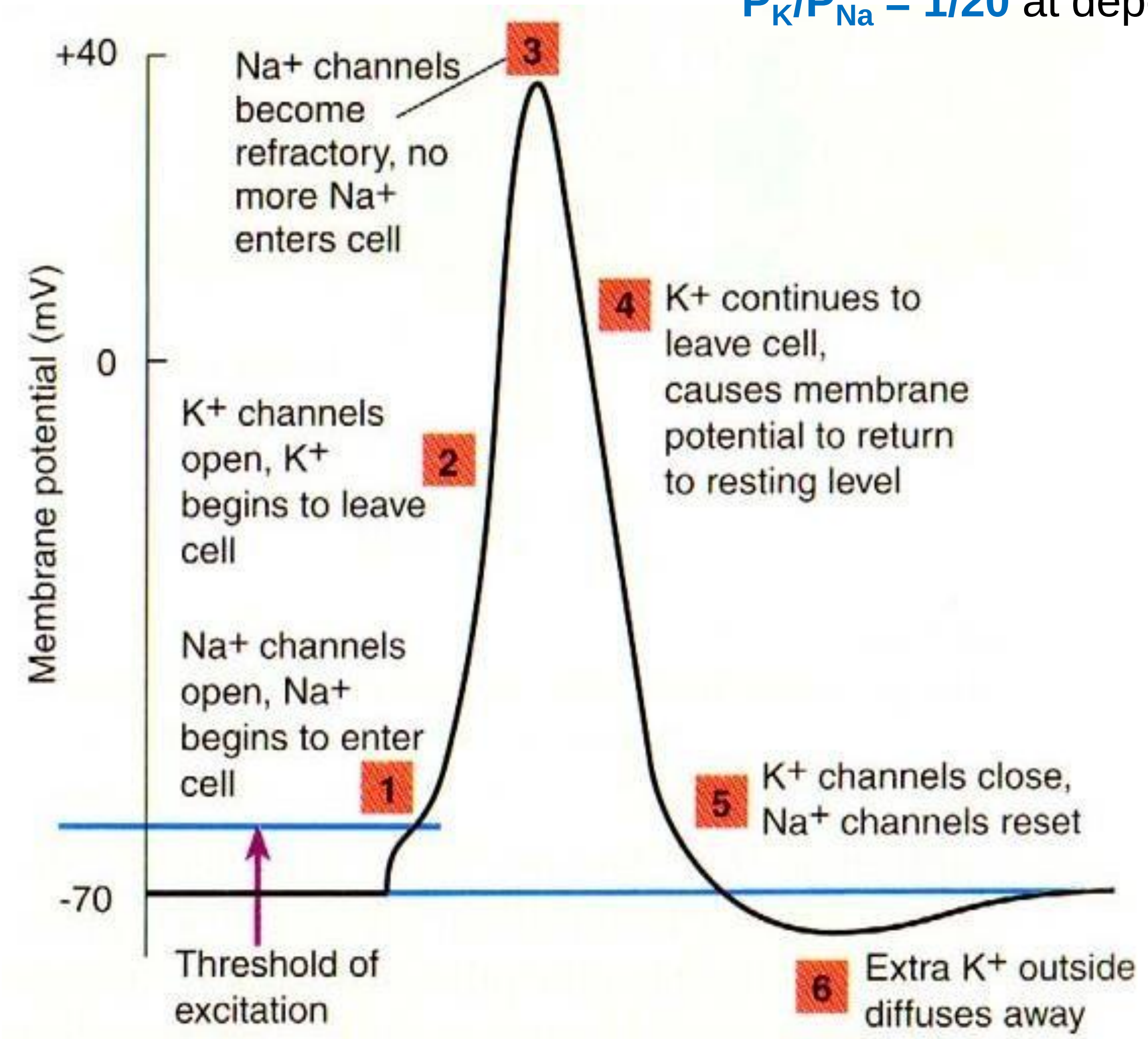




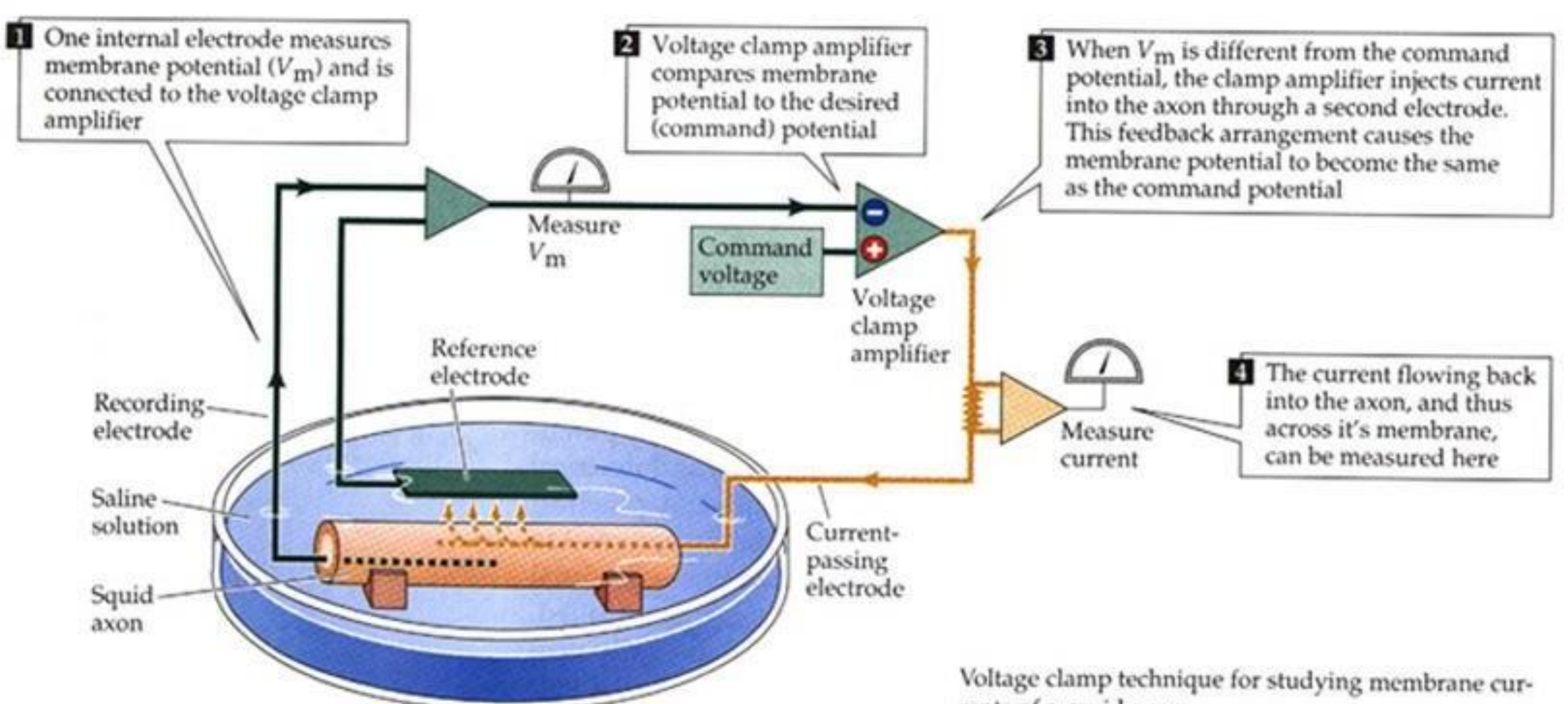
Configuration of an action potential. (**A**) Phases of an action potential. (**B**) Inward and outward current flows due to the influx of Na^+ (sodium) and efflux of K^+ (potassium) during the rising and falling phases of the action potential, respectively.

P_K/P_{Na} = **1/0.04** at resting membrane pot.

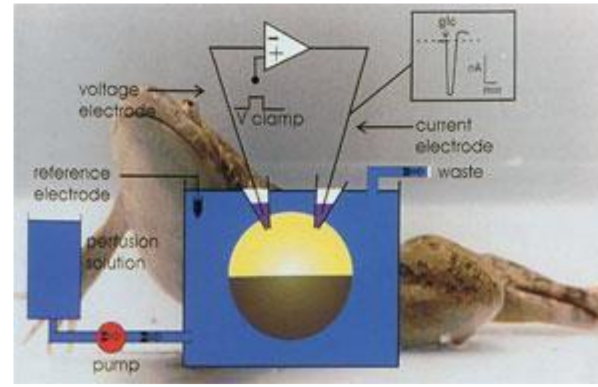
P_K/P_{Na} = **1/20** at depolarization phase

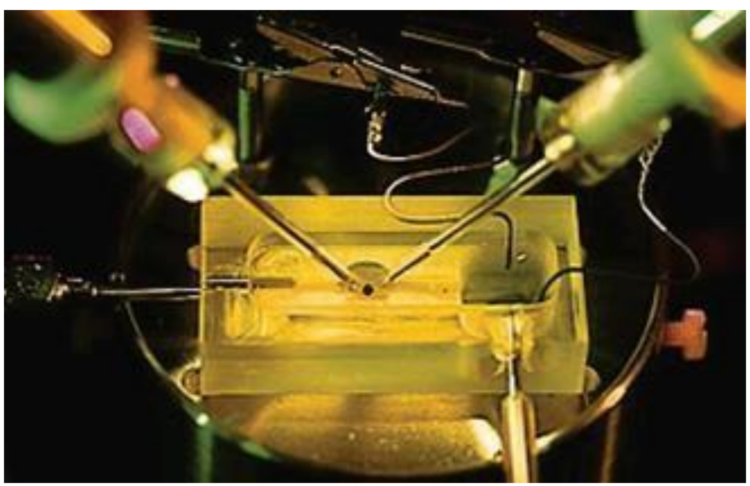


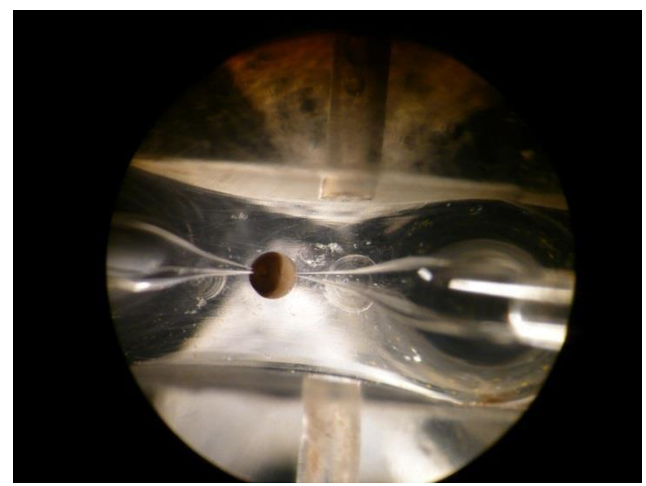
Voltage-Clamp Technique



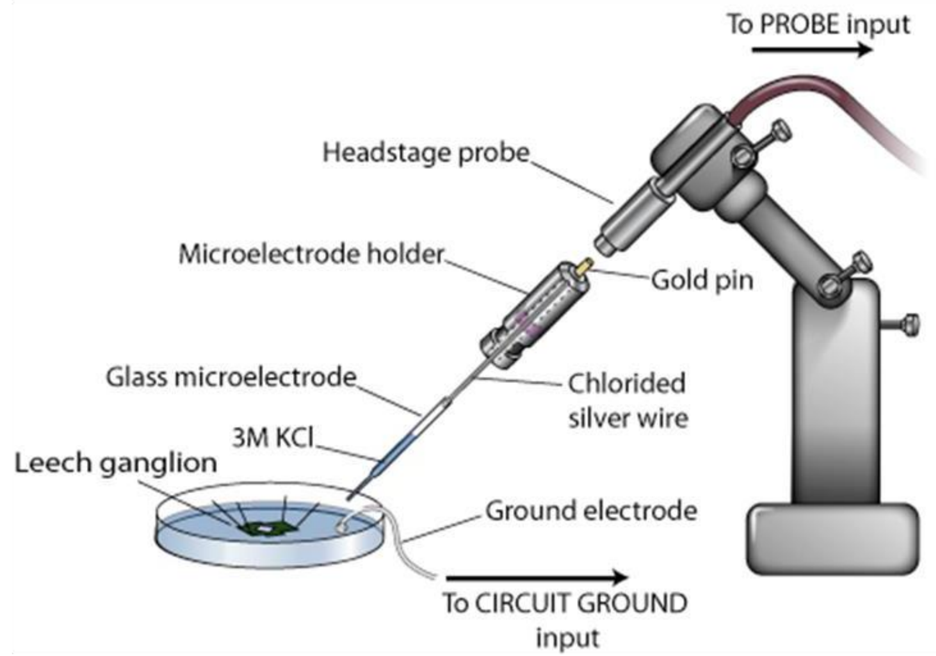
Voltage clamp technique for studying membrane currents of a squid axon.

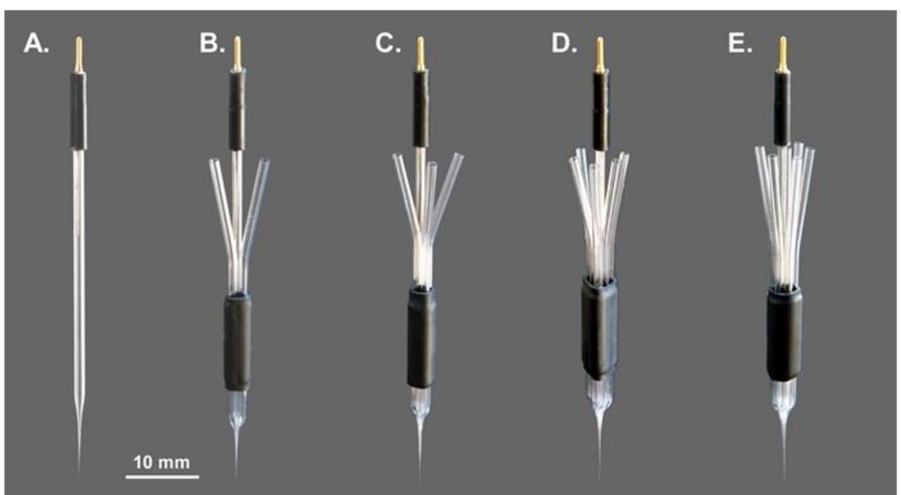

voltage
electrode
clamp
current
electrode
reference
electrode
waste
perfusion
solution
pump

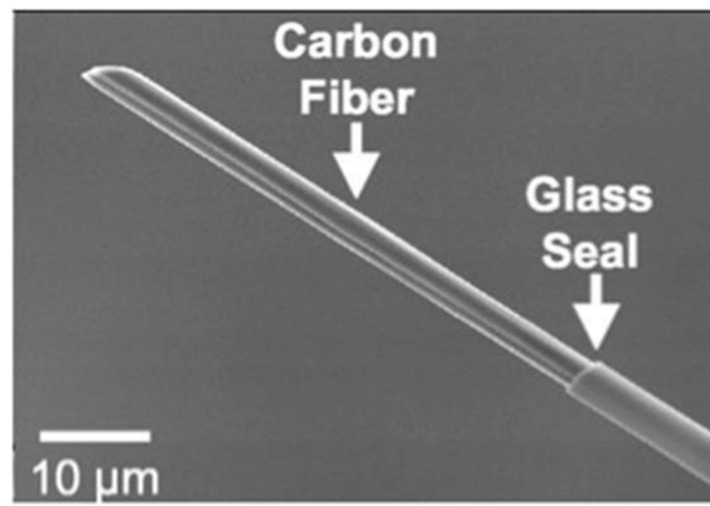




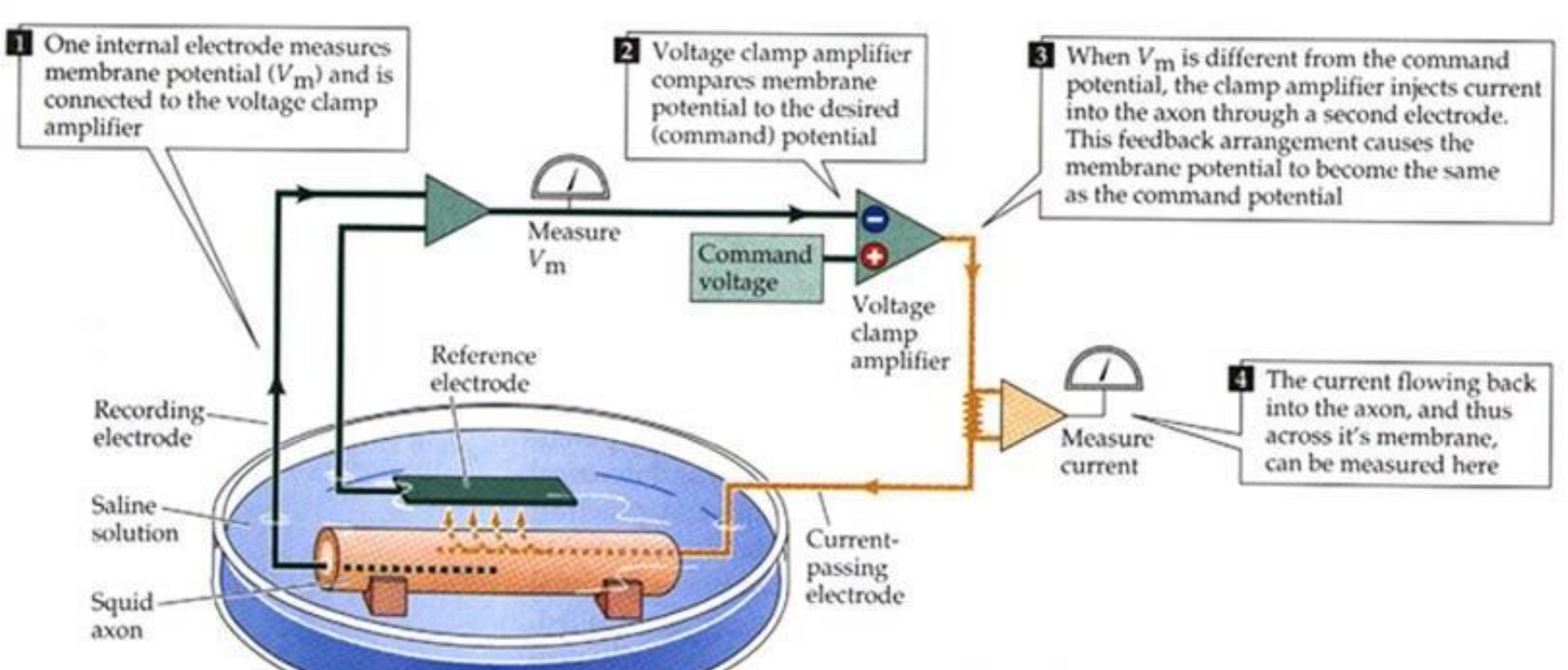

SUTTER INSTRUMENT CO.


To PROBE input
Headstage probe
Microelectrode holder
Gold pin
Glass microelectrode
Chlorided silver wire
3M KCl
Leech ganglion
Ground electrode
To CIRCUIT GROUND input

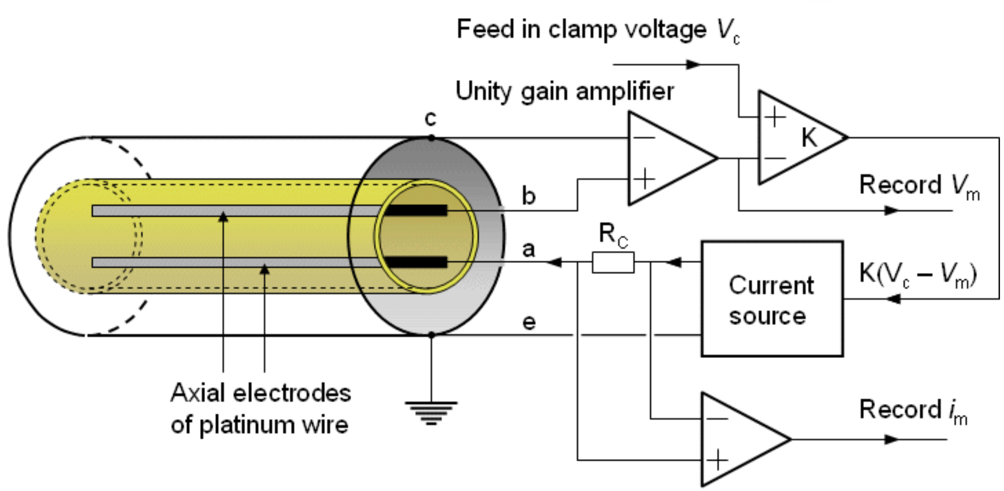

A.
B.
C.
D.
E.
10 mm


Carbon Fiber
Glass Seal
10 µm

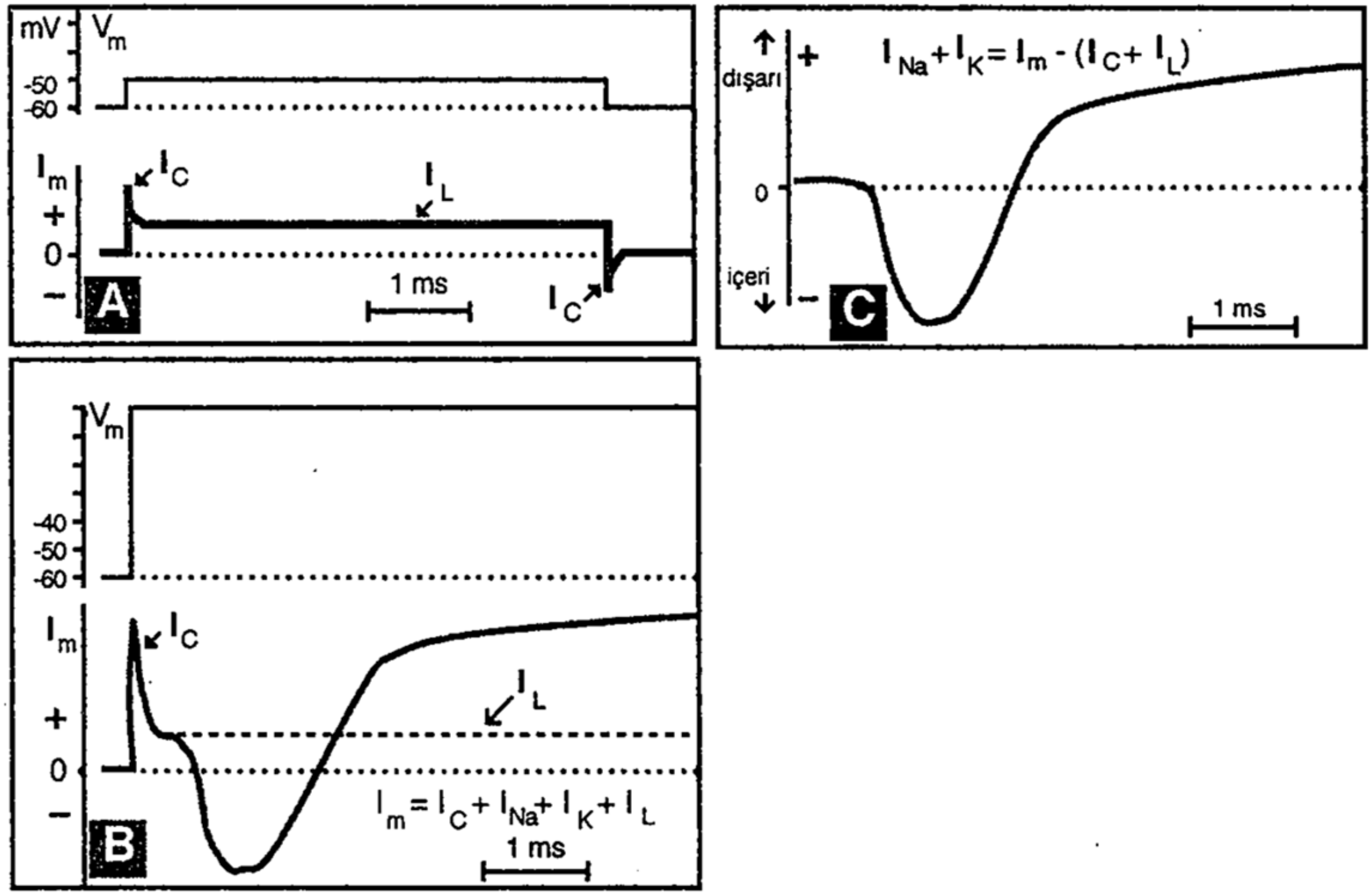
Basic Principle of the Technique



Voltage clamp technique for studying membrane currents of a squid axon.

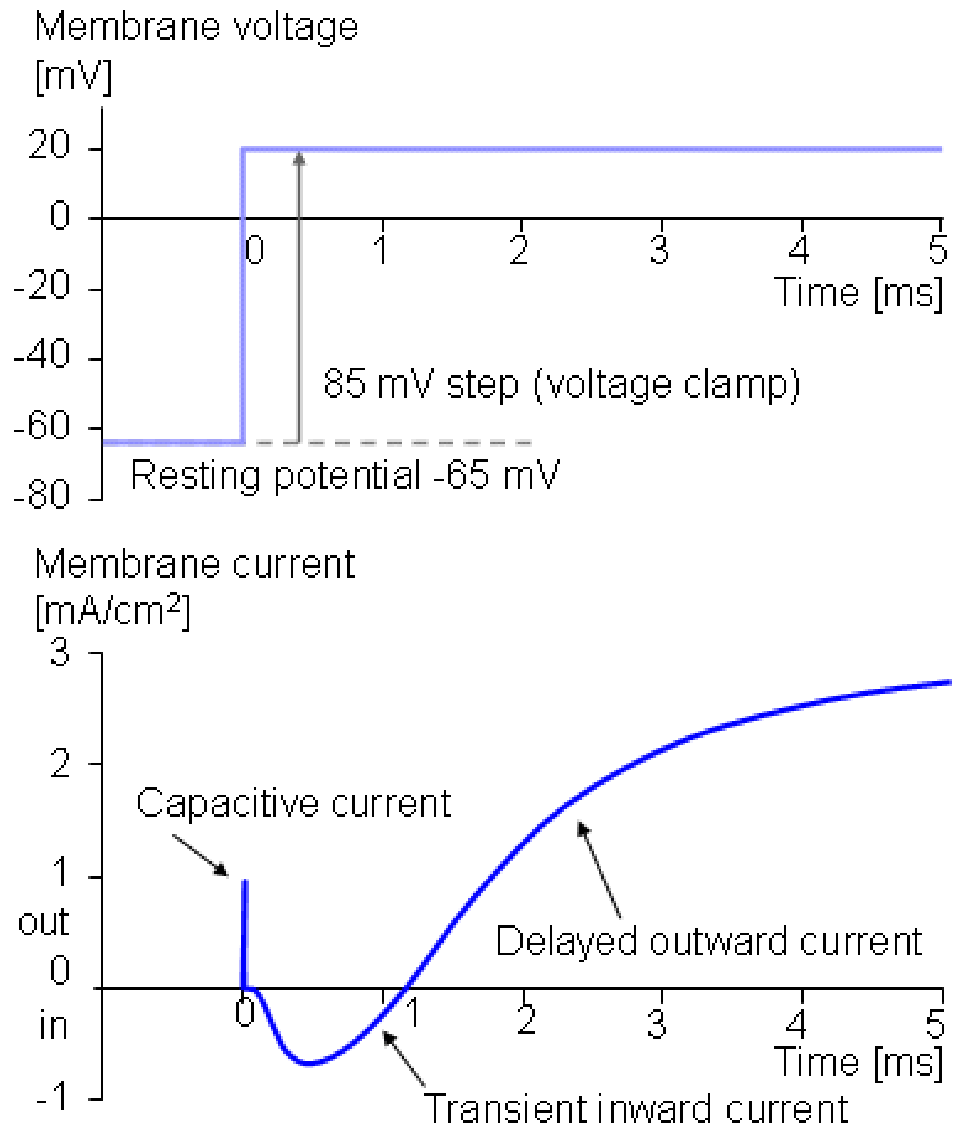


Components of the Total Membrane Current

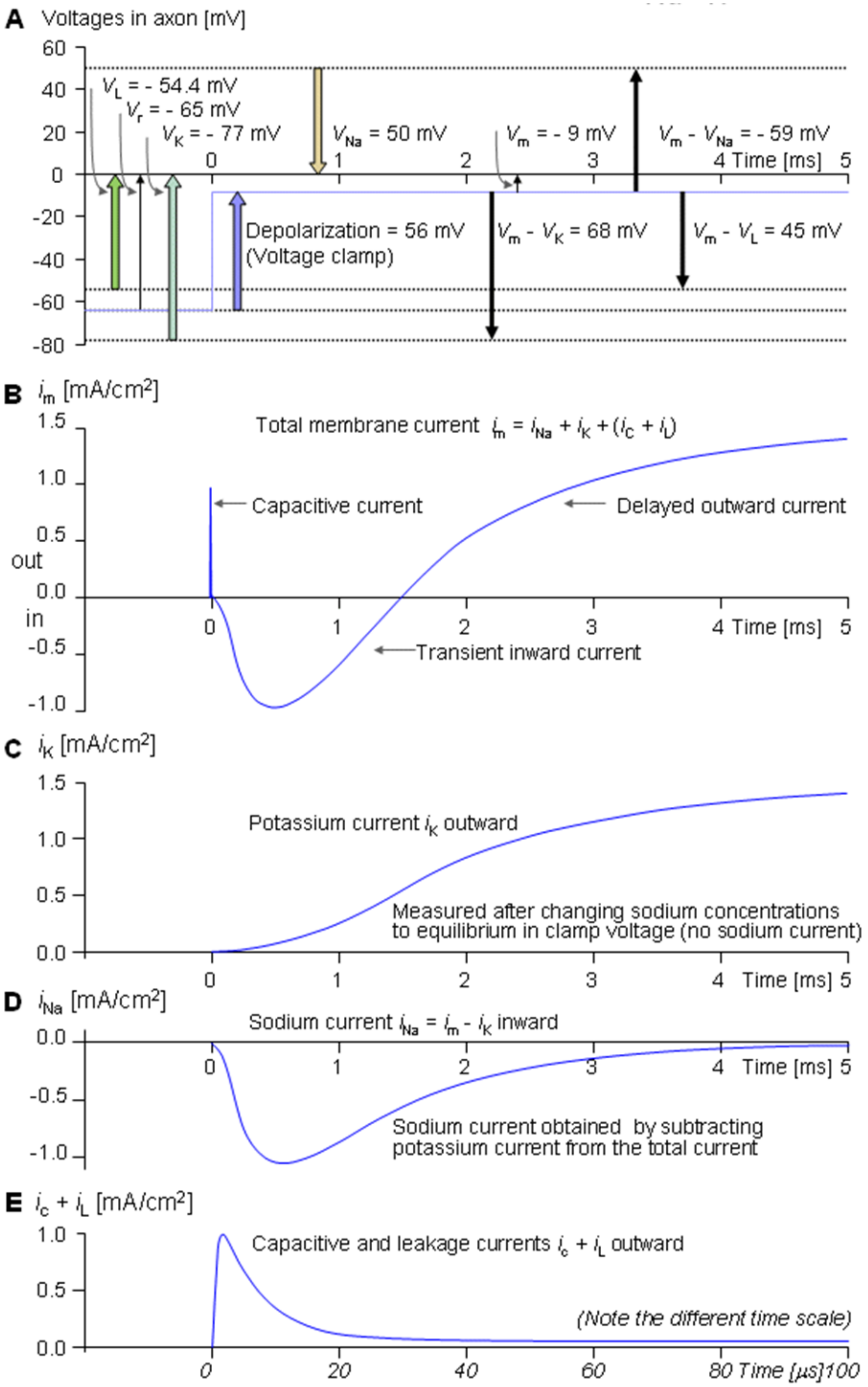


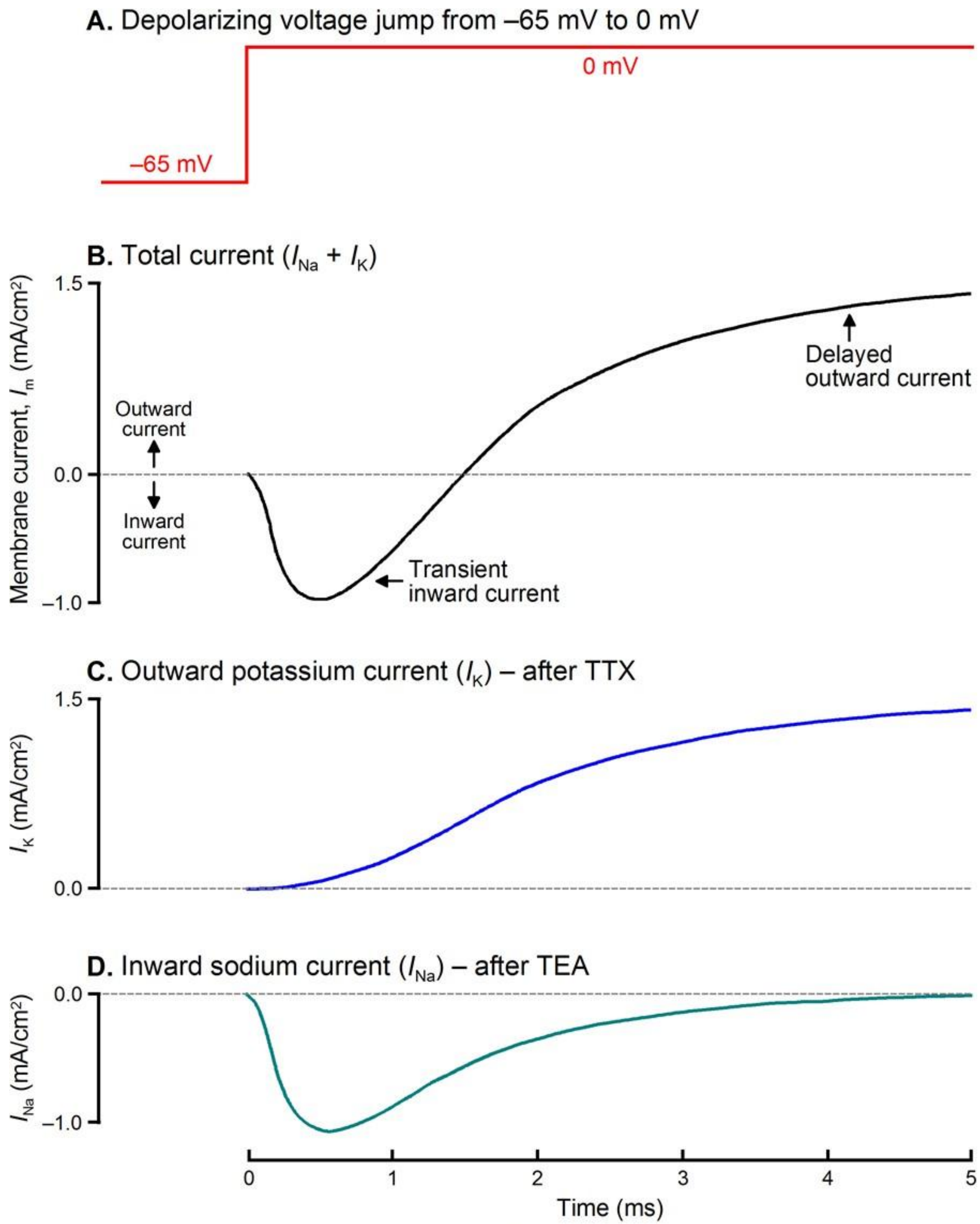
Potential inside the membrane

Measured trans-membrane current

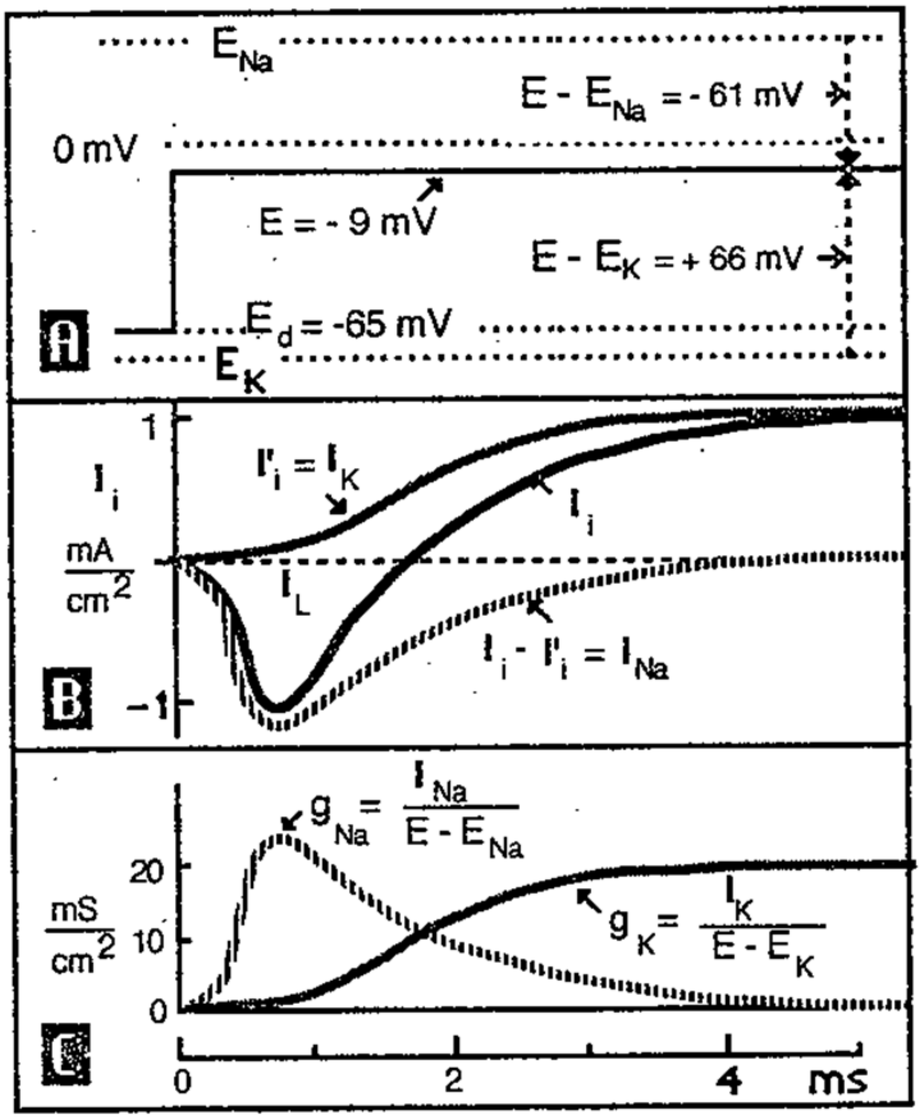


Separation of Sodium & Potassium Currents




A. Depolarizing voltage jump from –65 mV to 0 mV
0 mV
–65 mV
B. Total current (I_{Na} + I_K)
Membrane current, I_m (mA/cm²)
1.5
0.0
–1.0
Outward current
Inward current
Delayed outward current
Transient inward current
C. Outward potassium current (I_K) – after TTX
I_K (mA/cm²)
1.5
0.0
D. Inward sodium current (I_{Na}) – after TEA
I_{Na} (mA/cm²)
0.0
–1.0
0
1
2
3
4
5
Time (ms)

Conductance of A Voltage-gated Channel



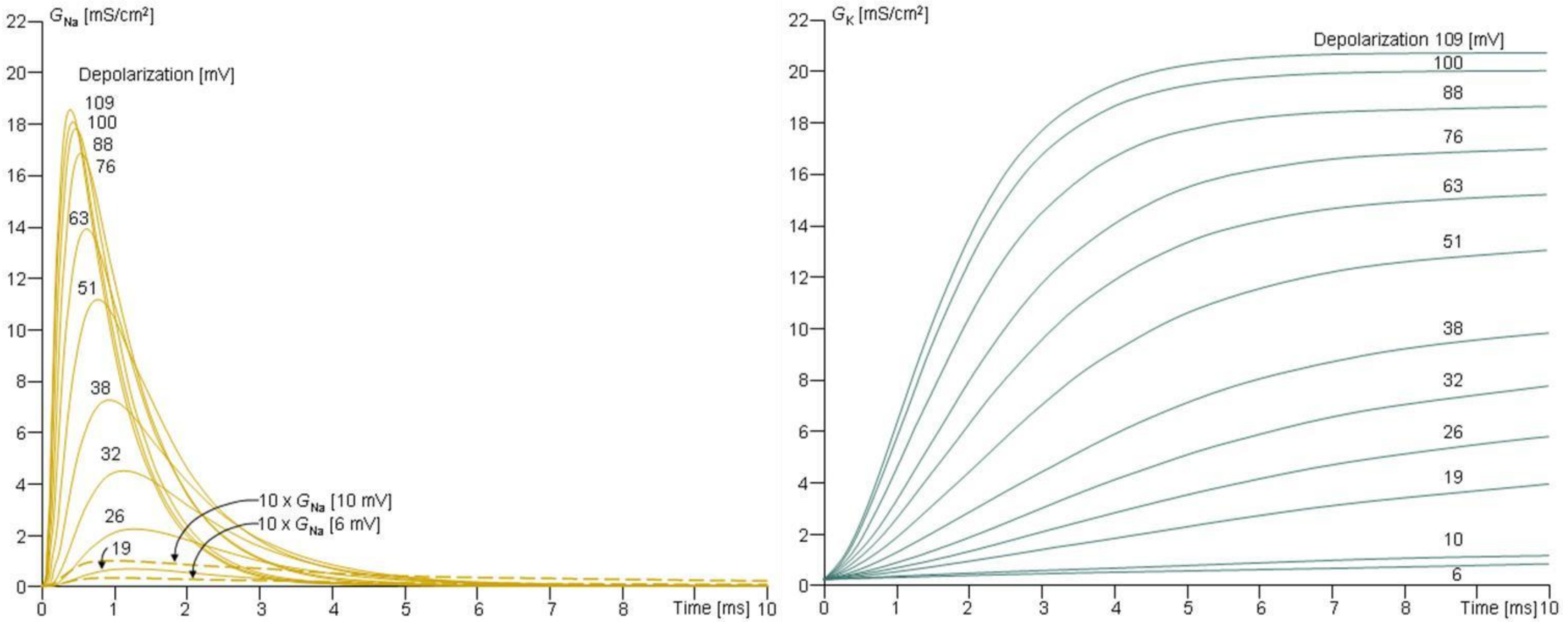
Electrical conductance:

The ability of an electrical charge to move from one point to another is determined by its electrical conductance (g). It is measured in siemens (S).

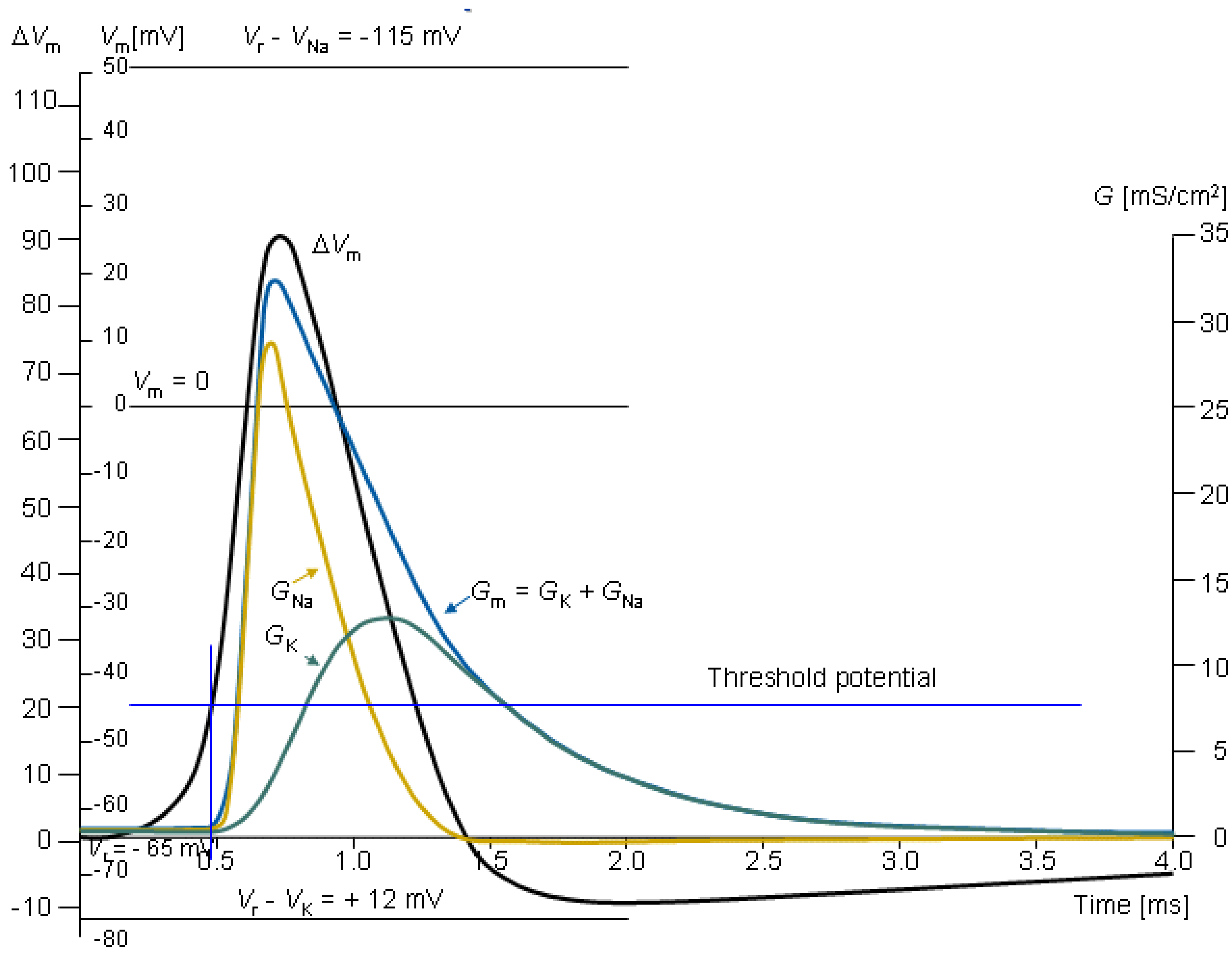
Ohms law:

This law describes the relationship between electrical current (I), electrical conductance (g), and electrical potential (V). According to this law, current is the product of the conductance and potential difference (I = gV).

The single-channel conductance (g) of typical ion channels ranges from 0.1 to 100 pS (picoSiemens).

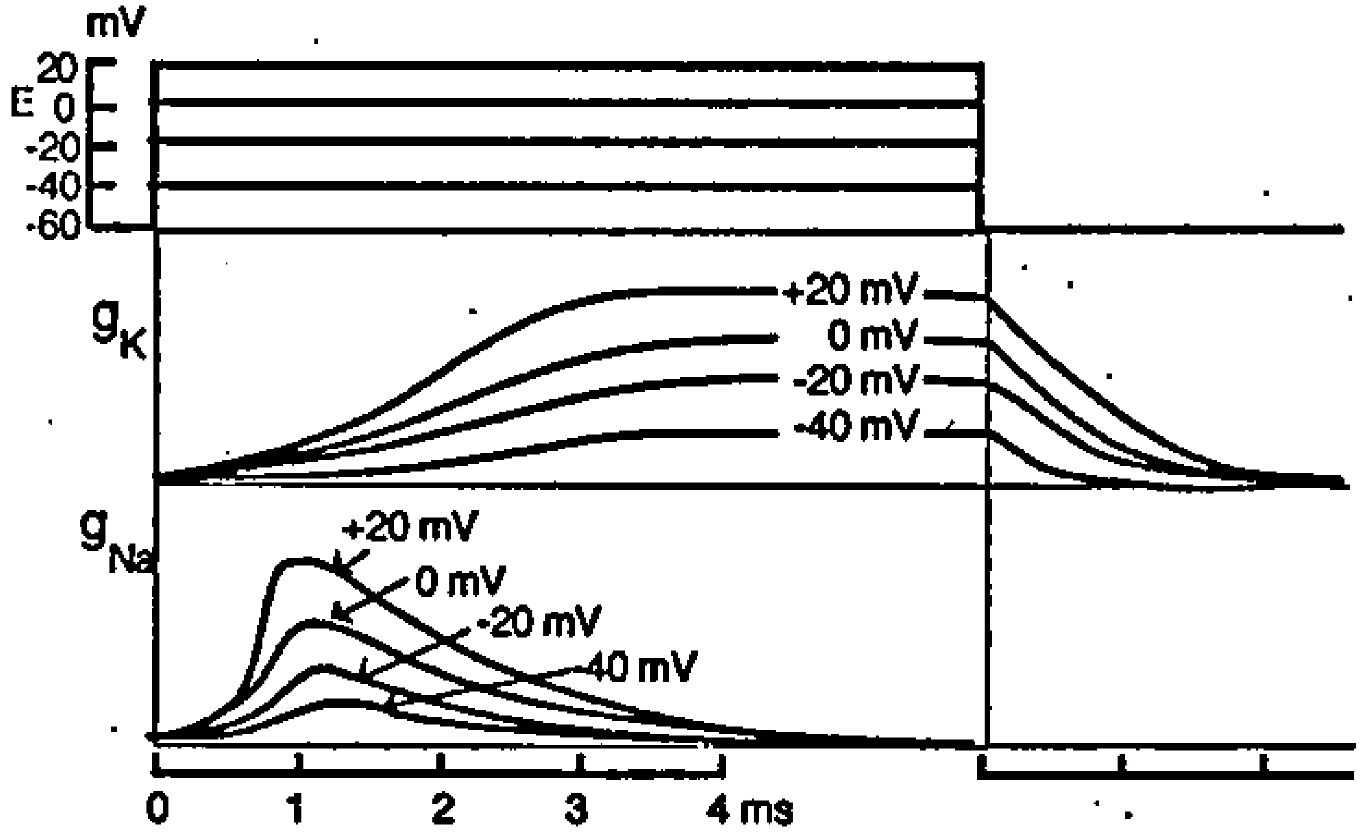


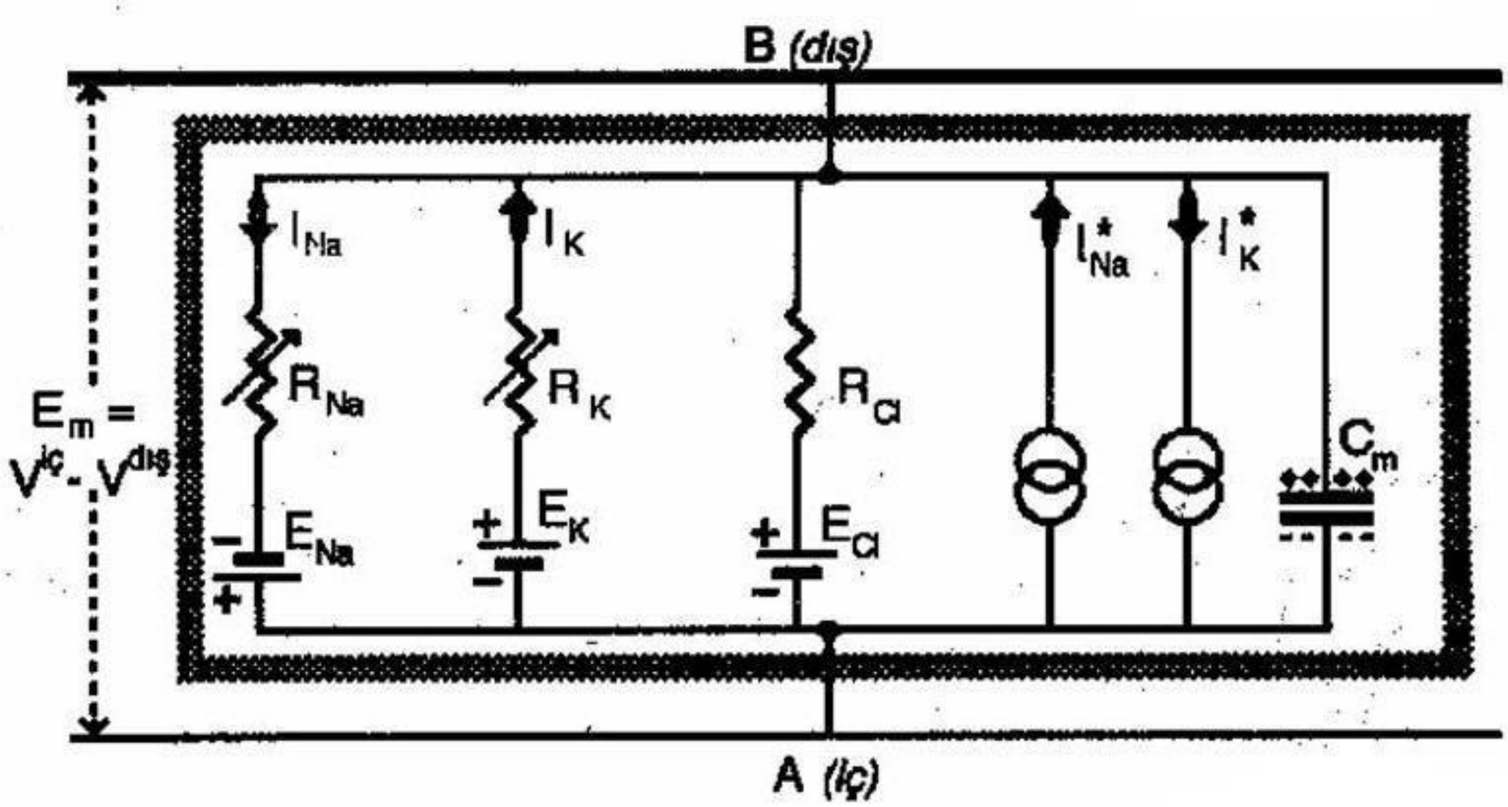
- The single-channel conductance of a;
  - Na_V channel ranges from 2 to 10 pS.
  - K_V channel ranges 4 – 14 pS.



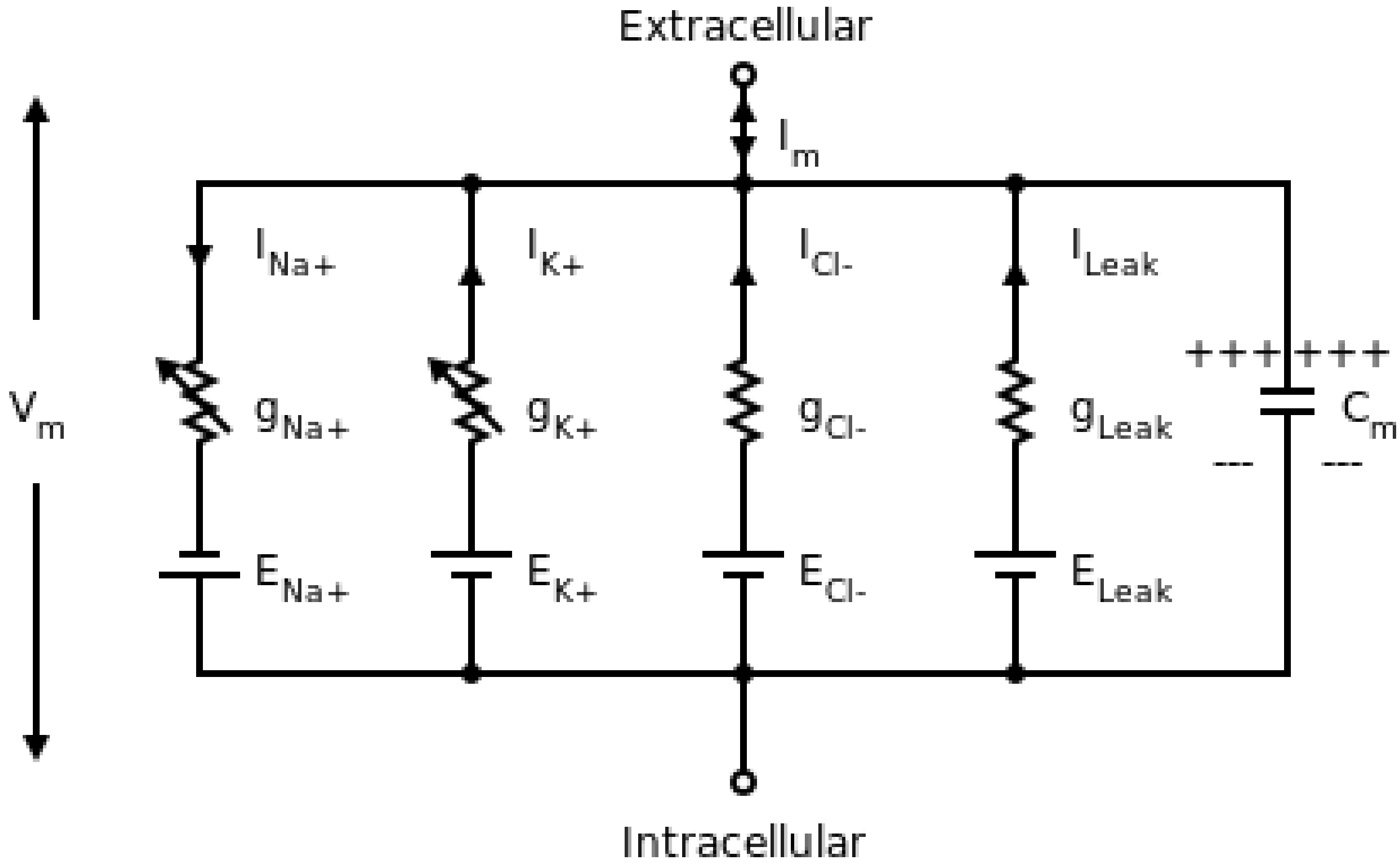
ΔV_m
V_m[mV]
V_r - V_{Na} = -115 mV
ΔV_m
V_m = 0
G_{Na}
G_K
G_m = G_K + G_{Na}
G [mS/cm²]
Threshold potential
V_r = - 65 mV
V_r - V_K = + 12 mV
Time [ms]

Two Similarities - Two Differences

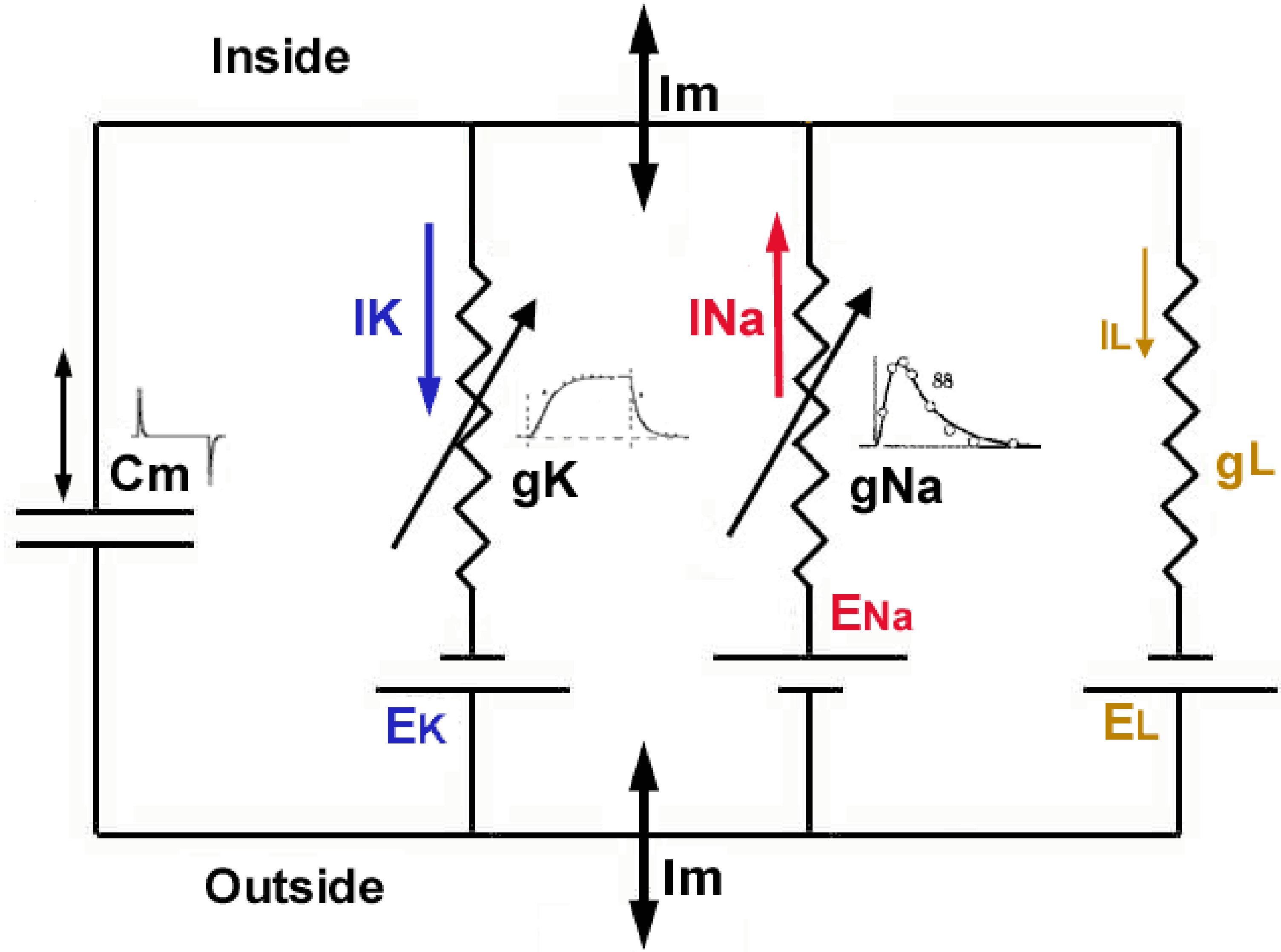




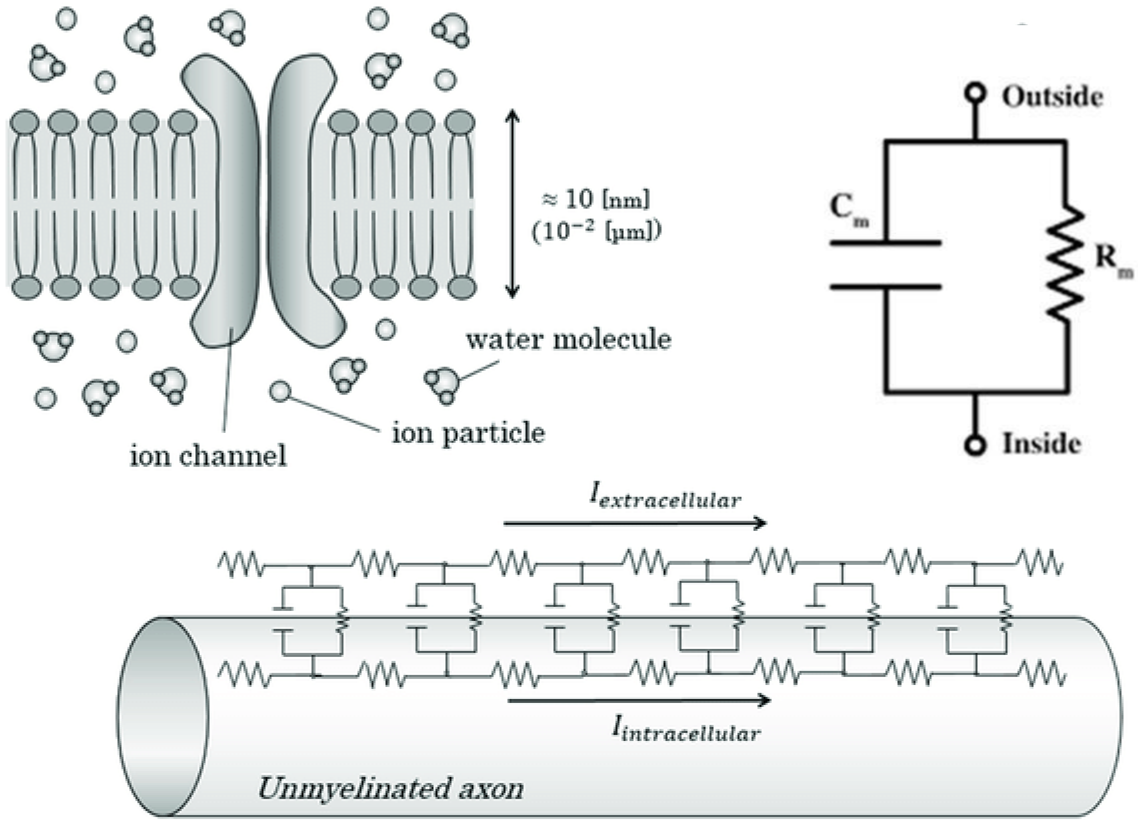
Electrical equivalent circuit for a whole cell membrane in resting

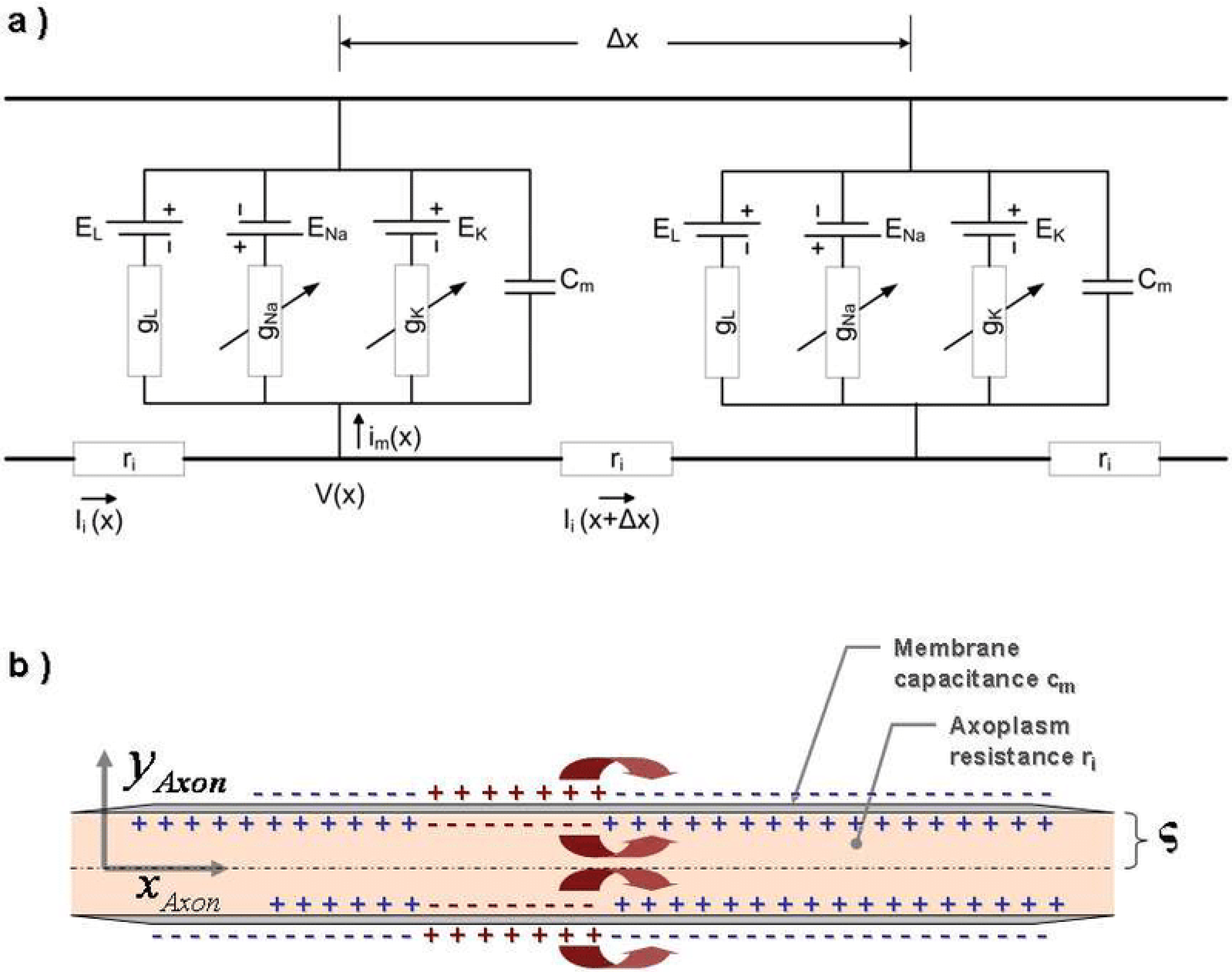


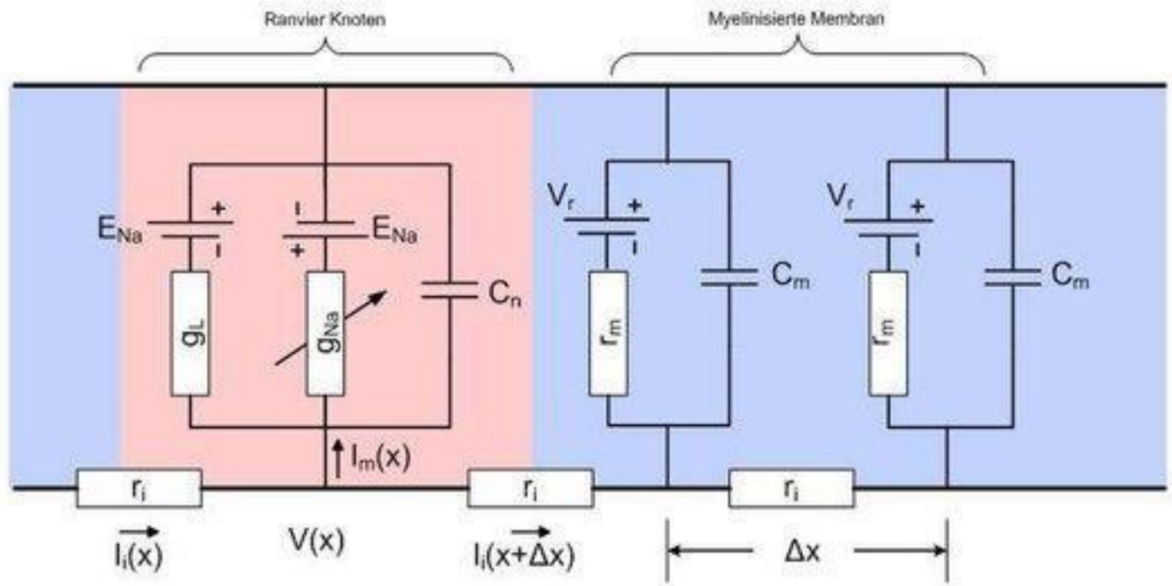
$$\boxed{g_i(conductance; ohm^{-1} or\ Siemens) = \frac{1}{R_i}}$$



$$E_m = \frac{g_K E_K + g_{Na} E_{Na} + g_L E_L}{g_K + g_{Na} + g_L}$$

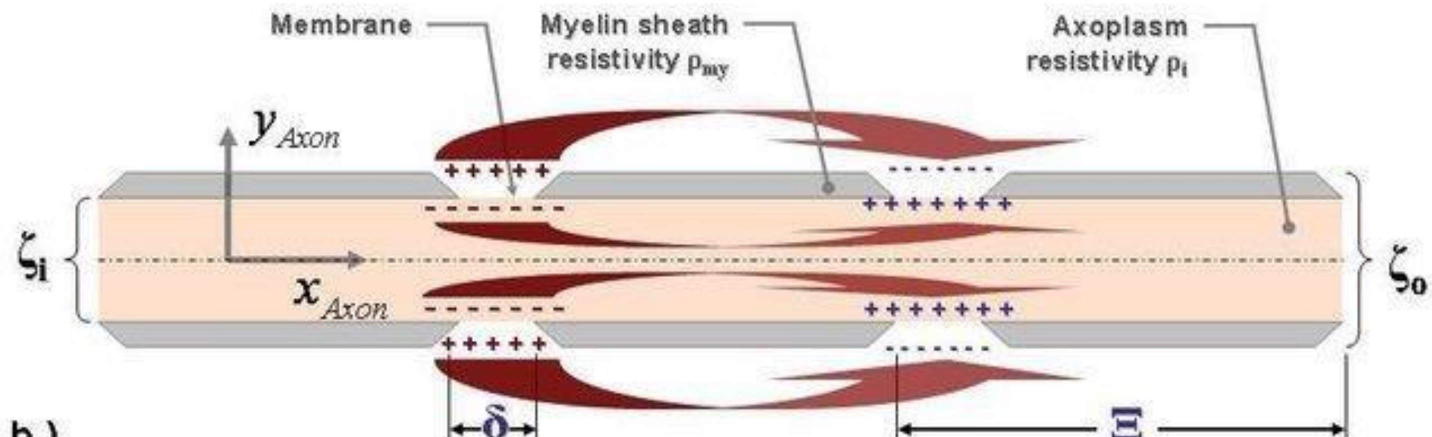

≈ 10 [nm]
(10⁻² [µm])
water molecule
ion particle
ion channel
Outside
C_m
R_m
Inside
I_extracellular
I_intracellular
Unmyelinated axon


a)
Δx
E_L
E_Na
E_K
C_m
g_L
g_Na
g_K
i_m(x)
r_i
V(x)
I_i (x)
I_i (x+Δx)
b)
Membrane capacitance c_m
Axoplasm resistance r_i
y_Axon
x_Axon
ς



Ranvier Knoten
Myelinisierte Membran
E_{Na}
g_L
g_{Na}
C_n
V_r
r_m
C_m
$I_m(x)$
r_i
$\overrightarrow{I_i(x)}$
$V(x)$
$\overrightarrow{I_i(x+\Delta x)}$
Δx

a)



Membrane
Myelin sheath resistivity ρ_{my}
Axoplasm resistivity ρ_i
y_{Axon}
x_{Axon}
ζ_i
ζ_o
δ
Ξ

b)

References

1. Pehlivan F. Biyofizik. Hacettepe-Taş, Ankara, 1997.
2. Siegel A., Sapru H.N. Essential Neuroscience. 2nd Edition. Lippincott Williams & Wilkins, 2011.
3. Hacker M., Bachman K., Messer Pharmacology: Principles & Practice. Academic Press, Elsevier, 2009.
4. Purves D., Augustine G.J., Fitzpatrick D., Hall W.C. Neuroscience. 3rd Ed., Sinauer Associates, Inc., 2004.